



SNS COLLEGE OF ALLIED HEALTH SCIENCE
SNS Kalvi Nagar, Coimbatore - 35
Affiliated to Dr MGR Medical University, Chennai



DEPARTMENT OF OPERATION THEATRE AND ANAESTHESIA
TECHNOLOGY - II YEAR

COURSE NAME: PHARMACOLOGY

TOPIC - DIURETICS

MRS.GAYATHIRI.K
Lecturer



DIURETICS



Introduction to Diuretics

- Diuretics are medications that increase urine production and volume by promoting the excretion of water and electrolytes, primarily through effects on the kidneys.
- They are essential in managing conditions involving fluid overload, such as heart failure, hypertension, edema, and electrolyte imbalances.
- Key roles: Reduce blood volume, lower blood pressure, alleviate edema, and aid in toxin excretion.



DIURETICS



Classification of Diuretics

Osmotic Diuretics: e.g., Mannitol – Act by increasing tubular osmolarity to draw water into the lumen.

Loop Diuretics: e.g., Furosemide – Potent agents targeting the loop of Henle.

Thiazide Diuretics: e.g., Hydrochlorothiazide – Act on distal convoluted tubule; used for hypertension.

Potassium-Sparing Diuretics: e.g., Spironolactone – Block aldosterone effects; prevent potassium loss.

Carbonic Anhydrase Inhibitors: e.g., Acetazolamide – Inhibit bicarbonate reabsorption; used for glaucoma or altitude sickness.



DIURETICS



Pharmacology of Mannitol (Osmotic Diuretic)

Mechanism of Action: Increases plasma and tubular fluid osmolality, drawing water from tissues (e.g., brain, eyes) into the bloodstream and preventing renal reabsorption; inhibits countercurrent mechanism in the nephron.

Pharmacokinetics:

- Administered IV (poor oral absorption).

Indications:

- Reduce intracranial pressure (ICP) and cerebral edema (e.g., traumatic brain injury).
- Treat acute kidney injury (AKI) and promote excretion of toxins.
- Reduce intraocular pressure (IOP) in glaucoma.
- Diagnostic aid for glomerular filtration rate.



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Onset of Action:

- Diuresis: 1–3 hours after IV administration.
- Intracranial pressure (ICP) reduction: 15–30 minutes.
- Intraocular pressure (IOP) reduction: 30–60 minutes.

Duration of Action:

- Diuresis: 6–8 hours.
- ICP/IOP reduction: 3–8 hours.

Dosage:

- Cerebral edema/ICP: 0.25–1 g/kg IV bolus over 20–30 min; repeat every 6–8 hours as needed (max 2 g/kg/day).
- Oliguria/AKI: 50–200 g over 24 hours (0.25–0.5 g/kg bolus, then infusion).
- IOP reduction: 1.5–2 g/kg IV over 30–60 min.



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Adverse Effects and Contraindications of Mannitol

Adverse Effects:

- Electrolyte imbalances (e.g., hypernatremia, hypokalemia).
- Dehydration, volume depletion, and acute kidney injury if overused.
- Pulmonary edema in susceptible patients; bronchospasm (inhaled form).
- Rare: Thrombosis, confusion, or hemoptysis.

Contraindications:

- Anuria or severe renal impairment (risk of osmotic nephropathy).
- Severe pulmonary edema or congestive heart failure.
- Active intracranial bleeding or severe dehydration.
- Hypersensitivity to mannitol.

Monitoring: Serum osmolality, electrolytes, renal function; test dose in anuria.



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Pharmacology of Furosemide (Loop Diuretic)

Mechanism of Action: Inhibits the $\text{Na}^+ - \text{K}^+ - 2\text{Cl}^-$ cotransporter (NKCC2) in the thick ascending limb of the loop of Henle, blocking 25-30% of sodium reabsorption; disrupts tubuloglomerular feedback and causes vasodilation.

Pharmacokinetics:

- Available oral/IV/IM/SC
- Excreted primarily by kidneys; hepatic metabolism to glucuronide.

Indications:

- Edema in congestive heart failure, liver cirrhosis, nephrotic syndrome, renal disease.
- Acute pulmonary edema and hypertension.
- Forced diuresis for poisoning (e.g., salicylate).



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- **Onset of Action:**
 - IV: 5–15 minutes (peak effect ~30 min).
 - Oral: 30–60 minutes (peak effect 1–2 hours).
- **Duration of Action:**
 - IV: 2–3 hours.
 - Oral: 6–8 hours.
- **Dosage:**
- **Edema (HF, renal, hepatic):**
 - Oral: 20–80 mg/day .
 - IV: 20–40 mg bolus, repeat every 6–8 hours; continuous infusion 0.1–0.4 mg/kg/h for severe cases.
- **Hypertension:** Oral 40 mg twice daily, adjust based on response.
- **Acute pulmonary edema:** IV 40–80 mg, repeat as needed (max 200 mg/dose).
- Adjust in renal impairment; avoid rapid IV to reduce ototoxicity risk.



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Adverse Effects and Contraindications of Furosemide

Adverse Effects:

- Electrolyte imbalances (hypokalemia, hyponatremia, hypomagnesemia, metabolic alkalosis).
- Ototoxicity (hearing loss, especially with rapid IV).
- Dehydration, hypotension, gout, and hypersensitivity reactions.
- Rare: Cardiac arrhythmias, renal failure in overdose.

Contraindications:

- Anuria, severe electrolyte depletion (e.g., hypokalemia).
- Hypersensitivity (including sulfonamide allergy).
- Hepatic coma or severe hyponatremia.

Monitoring: Electrolytes, renal function, hearing; potassium supplementation often needed.



DIURETICS



Slide 8: Comparison Between Mannitol and Furosemide

Aspect	Mannitol (Osmotic)	Furosemide (Loop)
Site of Action	Proximal tubule and descending loop	Thick ascending limb of loop of Henle
Mechanism	Osmotic retention of water; no electrolyte reabsorption effect	Inhibits Na-K-2Cl cotransporter; increases Na, K, Cl excretion
Primary Uses	Reduce ICP/IOP, AKI, toxin excretion	Edema in HF/cirrhosis/renal disease, hypertension, pulmonary edema
Administration	Primarily IV	Oral/IV/IM/SC
Side Effects	Electrolyte imbalances, pulmonary edema	Hypokalemia, ototoxicity, metabolic alkalosis
Potency	Mild diuresis, focuses on water	High potency, significant electrolyte loss
Onset	IV: 15–60 min (ICP/IOP); 1–3 h (diuresis)	IV: 5–15 min; Oral: 30–60 min



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Clinical Applications and Considerations

Mannitol: Preferred in neurosurgical settings for ICP reduction; combine with furosemide for enhanced brain water reduction, but no added benefit in preventing nephrotoxicity.

Furosemide: First-line for acute HF decompensation; continuous infusion may be superior in severe cases; manage diuretic resistance with higher doses or combinations.

Interactions: Both can interact with drugs affecting electrolytes (e.g., furosemide with ACE inhibitors increases hypotension risk); mannitol may alter absorption of oral meds.

General Considerations: Monitor for dehydration and electrolytes; potassium-rich diet for furosemide users; avoid in severe renal failure without caution.



DIURETICS



Conclusion

- Diuretics like mannitol and furosemide are vital for managing fluid and pressure-related disorders through distinct mechanisms.
- Mannitol excels in acute osmotic effects for neurological/ocular conditions, while furosemide provides potent loop inhibition for cardiac/renal edema.
- Safe use requires monitoring adverse effects and tailoring to patient needs for optimal outcomes.



THANK YOU